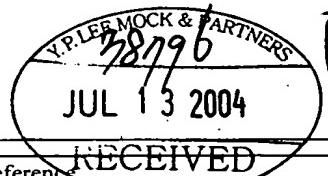


From the
INTERNATIONAL PRELIMINARY EXAMINING

PATENT COOPERATION TREATY

To:
LEE, Young-Pil

The Cheonghwa Building, 1571-18, Seocho-dong, Seocho-gu
137-874 Seoul Republic of Korea



PCT

WRITTEN OPINION

(PCT Rule 66)

9-6

Applicant's or agent's file reference YB-20069-PCT	RECEIVED	Date of mailing (day/month/year) <u>06 JULY 2004 (06.07.2004)</u>
International application No. PCT/KR2003/001502	International filing date (day/month/year) 26 JULY 2003 (26.07.2003)	Priority date(day/month/year) 26 JULY 2002 (26.07.2002)
International Patent Classification (IPC) or both national classification and IPC IPC7 C07D 405/12		
Applicant YUHAN CORPORATION et al		

1. This written opinion is the first (first,etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I Basis of the opinion
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

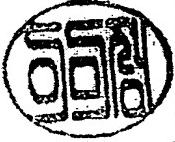
When ? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d)

How ? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3
For the form and the language of the amendments, see Rules 66.8 and 66.9

Also For an additional opportunity to submit amendments, see Rule 66.4
For an examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 16 NOVEMBER 2004 (16.11.2004)

Name and mailing address of the IPEA/KR  Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer LEE, Mi Jeong Telephone No. 82-42-481-5601	
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WRITTEN OPINION

International application No.

PCT/FR2003/001502

I. Basis of the opinion**1. With regard to the elements of the international application:*** the international application as originally filed the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

 the claims:

pages _____, as originally filed

pages _____, as amended (together with any statement) under Article 19

, filed with the demand

pages _____, filed with the letter of _____

 the drawings:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

 the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:** contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.**4. The amendments have resulted in the cancellation of:** the description, pages _____ the claims, Nos. _____ the drawings, sheet/fig _____**5.** This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.

PCT/KR2003/001502

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 10	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1 - 10	NO
Industrial applicability (IA)	Claims	1 - 10	YES
	Claims		NO

2. Citations and explanations

국제조사보고서의 인용문헌을 아래와 같이 정의함.

D1: WO 00/38687 (2000. 07. 06)

1. 신규성

본원발명의 청구항 제1-10항은 화학식(I) 화합물과 그 중간체, 그들의 제조방법 및 화학식(I) 화합물을 함유하는 cathepsin K를 포함하는 시스테인 프로테아제 억제제용 약학 조성물을 청구하고 있으나, 본원 우선권 주장일 이전에 발행된 D1에도 특히 cathepsin K에 대해 선택성을 가지는 프로테아제 억제제로 유용한 화학식 I 화합물이 기재되어 있는 바, 본원발명 화합물의 치환기 R1, R2, R3가 C1-6알킬인 경우의 화합물은 D1 화합물의 치환기 R", R'"이 수소, R2가 아릴-CO-6알킬, R1이 R4NR'R3CO-이고, R3가 아릴기, R'이 수소, R4가 R5CO-, R5가 알킬기인 화합물과 비교해 볼 때 본원의 사이클로헥실기가 D1에서는 아릴기이고 본원의 N 함유 헤테로 6원환이 D1에서는 7원환이라는 점에서 차이를 보이므로 본원 상기 청구항들의 D1에 대한 신규성은 인정됩니다(Article 33(2) PCT).

2. 진보성

본원발명의 화학식(I) 화합물과 D1의 화합물은 앞서 1. 신규성 부분에서 살펴본 바와 같은 치환기 차이를 가지고 있으나, 당업자라면 이 정도의 치환기 차이는 용이하게 예상할 수 있는 것으로 인정되고, 본원 화합물의 cathepsin K에 대한 선택성이나 생체이용률이 D1 화합물에 비해 현저히 우수하다고 인정할만한 비교시험결과 등의 자료도 없으므로 본원 상기 청구항들은 D1에 대한 진보성이 인정되지 않습니다 (Article 33(3) PCT).